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NEWS	3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	5	JAN 28	MARPAT searching enhanced
NEWS	6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	9	FEB 08	STN Express, Version 8.3, now available
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NEWS	11	FEB 25	IFIREF reloaded with enhancements
NEWS	12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS	13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS	14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS	17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	22	APR 28	IMSRESEARCH reloaded with enhancements
NEWS	23	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS	24	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS	25	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS	26	JUN 06	KOREAPAT updated with 41,000 documents
NEWS	27	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS	28	JUN 19	CAS REGISTRY includes selected substances from web-based collections

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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FILE 'HOME' ENTERED AT 11:11:04 ON 19 JUN 2008

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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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DICTIONARY FILE UPDATES:  18 JUN 2008  HIGHEST RN 1029146-45-9

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=> s AWD-12281
           186 AWD
            95 12281
L1           0 AWD-12281
                 (AWD(W)12281)

=> s loteprednol/cn
L2           1 LOTEPREDNOL/CN

=> d L2 str cn rn

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2008 ACS on STN

Absolute stereochemistry.
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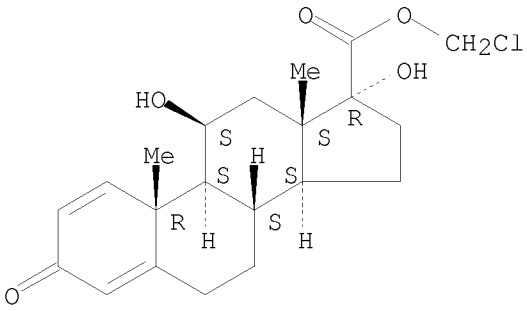

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Androsta-1,4-diene-17-carboxylic acid, 11,17-dihydroxy-3-oxo-, chloromethyl ester, (11β,17α)- (CA INDEX NAME)
OTHER NAMES:
CN Loteprednol
RN 129260-79-3 REGISTRY

=> s AWD12281
L3 0 AWD12281

=> file caplus medline embase biosis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.52	23.73

FILE 'CAPLUS' ENTERED AT 11:12:39 ON 19 JUN 2008
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=> s AWD12281
L4 2 AWD12281

=> dup rem L4
PROCESSING COMPLETED FOR L4
L5 2 DUP REM L4 (0 DUPLICATES REMOVED)

=> d 1-2 L5 ibib abs

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1267950 CAPLUS
DOCUMENT NUMBER: 144:266281
TITLE: AWD-12-281 (inhaled) Elbion/GlaxoSmithKline
AUTHOR(S): Gutke, Hans-Juergen; Guse, Jan-Hinrich; Khobzaoui, Moussa; Renukappa-Gutke, Thejavathi; Burnet, Michael
CORPORATE SOURCE: Synovo GmbH, Tubingen, D-72076, Germany
SOURCE: Current Opinion in Investigational Drugs (Thomson

Scientific) (2005), 6(11), 1149-1158
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Elbion (formerly ASTA Medica) and GlaxoSmithKline are developing an inhaled formulation of AWD-12-281 for the potential treatment of chronic obstructive pulmonary disease (COPD). By May 2005, phase II trials of this 5-hydroxyindole PDE4 inhibitor for COPD were ongoing.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:695438 CAPLUS
DOCUMENT NUMBER: 140:87294
TITLE: AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in the prevention and treatment of inflammatory reactions in a model of allergic dermatitis
AUTHOR(S): Baeumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Rundfeldt, Chris; Kietzmann, Manfred
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, School of Veterinary Medicine, Hannover, D-30559, Germany
SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(8), 1107-1114
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a phosphodiesterase 4 inhibitor, which is optimized for topical administration, was tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by topical administration of TDI onto the mice ears. AWD 12-281 was tested for its anti-inflammatory potential by oral, i.p. and topical administration. The phosphodiesterase 4 inhibitor, cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate, were used as reference compds. Given orally and i.p. 2 h before as well as 5 and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4, interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be potent in the prevention and treatment of allergic/inflammatory skin diseases.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s AWD 12-281
L6 107 AWD 12-281

=> dup rem L6
PROCESSING COMPLETED FOR L6

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L7           75 DUP REM L6 (32 DUPLICATES REMOVED)

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'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
   2 FILES SEARCHED...
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
L8           27 L7 AND (AY<2003 OR PY<2003 OR PRY<2003)

=> s allergy or allergic or dermatitis
L9       552456 ALLERGY OR ALLERGIC OR DERMATITIS

=> s L7 and L9
L10          30 L7 AND L9

=> s L8 and L10
L11          11 L8 AND L10

=> d 1-11 L11 ibib abs

L11  ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2004:60309  CAPLUS
DOCUMENT NUMBER:          140:105273
TITLE:                    Topical treatment of skin diseases
INVENTOR(S):              Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann,
                          Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen,
                          Norbert
PATENT ASSIGNEE(S):       Elbion AG, Germany
SOURCE:                   PCT Int. Appl., 48 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004006920         A1    20040122    WO 2003-EP7514          20030710 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 20040038958        A1    20040226    US 2003-611649          20030701 <--
     CA 2492093            A1    20040122    CA 2003-2492093         20030710 <--
     AU 2003254332         A1    20040202    AU 2003-254332          20030710 <--
     BR 2003012696         A     20050426    BR 2003-12696           20030710 <--
     EP 1531818            A1    20050525    EP 2003-763810          20030710 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     CN 1681500            A     20051012    CN 2003-821520          20030710 <--
     JP 2005537262         T     20051208    JP 2004-520586          20030710 <--
     NZ 537482             A     20060929    NZ 2003-537482          20030710 <--
     ZA 2005000108         A     20050223    ZA 2005-108             20050106 <--
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MX 2005PA00486 A 20050722 MX 2005-PA486 20050111 <--
NO 2005000718 A 20050401 NO 2005-718 20050210 <--
PRIORITY APPLN. INFO.: US 2002-395221P P 20020711 <--
WO 2003-EP7514 W 20030710

OTHER SOURCE(S): MARPAT 140:105273

AB The present invention relates to a method for the treatment of an inflammatory and/or allergic skin disease comprising topically administering a substituted hydroxy indole which is a phosphodiesterase 4 inhibitor. Examples are provided of the topical effectiveness of AWD 12-281 and cilomilast in dermal immunol. inflammation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:495906 CAPLUS

DOCUMENT NUMBER: 138:117605

TITLE: Effects of the phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on the inflammatory reaction in a model of allergic dermatitis

AUTHOR(S): Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Ehinger, Britt; Kietzmann, Manfred

CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany

SOURCE: European Journal of Pharmacology (2002), 446(1-3), 195-200
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by topical administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups of mice were treated topically (ear skin) with SB 207499 or AWD 12-281. There was a significant ear swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB 207499 and AWD 12-281 inhibited this swelling significantly 8, 16, 24 and 48 h after the challenge. For biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited significantly the secretion of interleukin 1β induced by toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-281 and SB 204799.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:420229 CAPLUS

DOCUMENT NUMBER: 138:18980

TITLE: AWD 12-281

AUTHOR(S): Kuss, H.; Hofgen, N.; Egerland, U.; Heer, S.; Marx,

D.; Szelenyi, I.; Schupke, H.; Gasparic, A.; Olbrich, M.; Hempel, R.; Hartenhauer, H.; Krone, D.; Berthold, K.; Kronbach, T.; Rundfeldt, C.
CORPORATE SOURCE: Arzneimittelwerk Dresden GmbH, Radebeul, D-01445, Germany
SOURCE: Drugs of the Future (2002), 27(2), 111-116
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Airway diseases such as bronchial asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases whose prevalence is increasing. Current research concerned with developing effective treatments for these conditions have focused on the search for alternatives to the standard corticosteroid antiinflammatory therapy. Selective phosphodiesterase 4 (PDE4) inhibitors have received a considerable amount of attention due to their ability to suppress the functions of several cell types involved in allergic and inflammatory disorders. The selective PDE4 inhibitor AWD 12-281 is the result of a pharmacophore-based synthesis program wherein the optimization process was supported by ligand-based drug design methods. AWD 12-281 was selected for further development for its high affinity and selectivity for the human PDE4 isoenzyme and due to its potent activity and excellent tolerability in models of allergic rhinitis, asthma and COPD, especially after topical treatment.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:30560 CAPLUS
DOCUMENT NUMBER: 134:221365
TITLE: The effect of selective and non-selective phosphodiesterase inhibitors on allergen- and leukotriene C4-induced contractions in passively sensitized human airways
AUTHOR(S): Schmidt, Dunja T.; Watson, Nikki; Dent, Gordon; Ruhlmann, Elke; Branscheid, Detlev; Magnussen, Helgo; Rabe, Klaus F.
CORPORATE SOURCE: Department of Pulmonology, Leiden University Medical Centre, Leiden, NL-2333 ZA, Neth.
SOURCE: British Journal of Pharmacology (2000), 131(8), 1607-1618
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Non-selective inhibitors of cyclic nucleotide phosphodiesterase (PDE) block allergen-induced contraction of passively sensitized human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of histamine and cysteinyl leukotriene (LT) release from airways. We investigated the effects of non-selective PDE inhibitors and selective inhibitors of PDE3 and PDE4 in order to determine the involvement of PDE isoenzymes in the suppression of allergic bronchoconstriction. Macroscopically normal airways from 76 patients were sensitized with IgE-rich sera (>250 u ml-1) containing specific antibodies against allergen (Dermatophagoides farinae). Contractile responses of bronchial rings were assessed using standard organ bath techniques. Passive sensitization caused increased contractile responses to allergen, histamine and LTC4. Non-selective PDE inhibitors (theophylline, 3-isobutyl-1-methylxanthine [IBMX]), a PDE3-selective inhibitor (motapizone), PDE4-selective inhibitors (RP73401, rolipram, AWD

12-281) and a mixed PDE3/4 inhibitor (zardaverine) all significantly relaxed inherent bronchial tone at resting tension and to a similar degree. Theophylline, IBMX, zardaverine and the combination of motapizone and RP73401 inhibited the contractile responses to allergen and LTC4. Pre-treatment with motapizone, RP73401, rolipram or the methylxanthine adenosine receptor antagonist, 8-phenyltheophylline, did not significantly decrease responses to either allergen or LTC4. We conclude that combined inhibition of PDE3 and PDE4, but not selective inhibition of either isoenzyme or antagonism of adenosine receptors, is effective in suppressing allergen-induced contractions of passively sensitized human airways. The relationship between allergen- and LTC4-induced responses suggests that PDE inhibitors with PDE3 and PDE4 selectivity are likely to act in part through inhibition of mediator release and not simply through direct relaxant actions on airway smooth muscle.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:647583 CAPLUS
DOCUMENT NUMBER: 132:145941
TITLE: Therapeutic potential of phosphodiesterase 4 inhibitors in allergic diseases
AUTHOR(S): Crocker, I. Caroline; Townley, Robert G.
CORPORATE SOURCE: Creighton University Allergic Disease Center, Omaha, NE, USA
SOURCE: Drugs of Today (1999), 35(7), 519-535
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 137 refs. CAMP is thought to be associated with inflammatory cell activity: high levels tend to decrease proliferation and cytokine secretion, whereas low concns. have the opposite effect (1). Since many phosphodiesterases (PDEs) degrade cAMP, inhibitors of this enzyme decrease inflammatory cell activity. Theophylline, which has nonselective PDE inhibitor activity in addition to its other mechanisms of action, has been used in the treatment of asthma for many years. Unfortunately, because of the important role of PDEs in the cell, nonspecific inhibition of these enzymes causes many undesirable side effects. The discovery of PDE isoenzyme families (PDE1-PDE10), their subtypes (HPDE4 and LPDE4) and their differential distribution among the cell types, as well as their specific functions in controlling cell processes, has led to the development of new, specific PDE4 inhibitors. This review details the rationale for the use of PDE4 inhibitors in the treatment of allergic disease. In addition, the effects of PDE4 inhibitors in vitro, in preclin. animal models and in the clinic are covered. Finally, up-to-date information on the most recently developed inhibitors, such as SB-207499, CDP-840, AWD-12-281 and D-4418, is provided.

REFERENCE COUNT: 137 THERE ARE 137 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003087901 EMBASE
TITLE: Respiratory drug development compendium 2002.
AUTHOR: Graul, A.I.
SOURCE: Drugs of the Future, (1 Dec 2002) Vol. 27, No. 12, pp. 1181-1194.
ISSN: 0377-8282 CODEN: DRFUD4

COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Mar 2003
Last Updated on STN: 25 Mar 2003

L11 ANSWER 7 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002315426 EMBASE
TITLE: Modulation of TNF and GM-CSF release from dispersed human nasal polyp cells and human whole blood by inhibitors of different PDE isoenzymes and glucocorticoids.
AUTHOR: Marx, Degenhard (correspondence); Tassabehji, Mahmoud; Heer, Sabine; Szelenyi, Istvan
CORPORATE SOURCE: Pulmonary Pharmacology, Corporate Research ASTA Medica AG, Arzneimittelwerk Dresden GmbH, Radebeul, Germany. degenhard.marx@byk.de
AUTHOR: Huttenbrink, K.-B.
CORPORATE SOURCE: Clinic of Otolaryngology, University of Dresden, Germany.
AUTHOR: Marx, Degenhard (correspondence)
CORPORATE SOURCE: Department of Pharmacology, Byk Gulden Str. 2, 78403 Konstanz, Germany. degenhard.marx@byk.de
SOURCE: Pulmonary Pharmacology and Therapeutics, (2002) Vol. 15, No. 1, pp. 7-15.
Refs: 55
ISSN: 1094-5539 CODEN: PPTHFJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 2002
Last Updated on STN: 19 Sep 2002

AB The aim of this study was to investigate the role of the inhibitors of different PDE isoenzymes (PDE 1-5) on the production of two pro-inflammatory cytokines - tumor necrosis factor alpha (TNF) and granulocyte-macrophage colony-stimulating factor (GM-CSF). Two in vitro models were used to compare the antiinflammatory properties of PDE inhibitors with that of glucocorticoids. The effect on TNF release from diluted human blood following lipopolysaccharide (LPS from Salmonella abortus equi) stimulation as well as the GM-CSF and TNF release from human nasal polyp cells following allergic stimulation were investigated. Both models proofed to be well suited for the characterisation of the antiinflammatory properties of new chemical entities. In diluted human blood and dispersed human nasal polyp cells the induced TNF release was most potently suppressed by selective PDE4 inhibitors. Amrinone and milrinone, selective PDE3 inhibitors, suppressed TNF secretion to a lesser extent. The effects of theophylline (unspecific PDE inhibitor), vinpocetine (PDE1 inhibitor), EHNA (PDE2 inhibitor) and the PDE5 inhibitors zaprinast and E 4021 were weak. In human blood, the tested glucocorticoids beclomethasone, dexamethasone and fluticasone inhibited the LPS induced TNF release potently in a concentration dependent manner, whereas in dispersed human nasal polyp cells, the effect of the glucocorticoids on allergically induced TNF release, with the exception of dexamethasone, was much less pronounced. Glucocorticoids were the most potent inhibitors of GM-CSF release and the effect correlates well with the affinity to the glucocorticoid receptor. The selective PDE 4 inhibitors, and to a certain extent the PDE3 inhibitors

amrinone and milrinone, reduced the GM-CSF release in a concentration dependent manner. In all investigations selective PDE4 inhibitors reduced TNF release to a much higher degree (4-10 fold) than GM-CSF release. .COPYRGT. 2002 Elsevier Science Ltd.

L11 ANSWER 8 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000413538 EMBASE
TITLE: Animal models of allergic rhinitis.
AUTHOR: Szelenyi, I., Dr. (correspondence); Marx, D.; Jahn, W.
CORPORATE SOURCE: Pulmonary Pharmacology (BF-FP2), Meissnerstr. 191, 01445 Radebeul, Germany. stefan.szelenyi@astamedica.de
SOURCE: Arzneimittel-Forschung/Drug Research, (2000) Vol. 50, No. 11, pp. 1037-1042.
Refs: 44
ISSN: 0004-4172 CODEN: ARZNAD
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 14 Dec 2000
Last Updated on STN: 14 Dec 2000
AB Actively sensitized Brown Norway rats and guinea pig are useful species for studying drug effects on symptoms of experimental rhinitis. Even if not all symptoms of human rhinitis can be induced and detected in the same animal species, the predictablity of methods generally used is well acceptable. In the present review, advantages and disadvantages of experimental methods of rhinitis will be discussed.

L11 ANSWER 9 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000403119 EMBASE
TITLE: PDE4 inhibitors and chronic obstructive pulmonary disease.
AUTHOR: Wolda, S.L. (correspondence)
CORPORATE SOURCE: ICOS Corporation, 22021 20th Ave SE, Bothell, WA 98021, United States. swolda@icos.com
SOURCE: Emerging Drugs, (2000) Vol. 5, No. 3, pp. 309-319.
Refs: 56
ISSN: 1361-9195 CODEN: EMDRFV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 13 Dec 2000
AB Inhibitors of the 3', 5' cyclic nucleotide phosphodiesterase Type IV (PDE4) are able to modulate a variety of inflammatory responses in both cell and animal based models. These results suggest that PDE4 inhibitors may provide a novel approach for treating chronic inflammatory diseases. A number of pharmaceutical companies are developing PDE4 inhibitors for the treatment of inflammatory diseases including asthma, rheumatoid arthritis, multiple sclerosis and Crohn's disease. Recent clinical evidence suggests that PDE4 inhibitors may also be efficacious in the

treatment of chronic obstructive pulmonary disease (COPD). This review will summarise current treatments for COPD, the scientific rationale for using PDE4 inhibitors to treat this disease and the current status of known PDE4 inhibitors.

L11 ANSWER 10 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000318467 EMBASE
TITLE: PDE4 inhibitors: Sustained patenting activity as leading drugs near the market.
AUTHOR: Norman, P. (correspondence)
CORPORATE SOURCE: 18 Pink Lane, Burnham, Bucks SL1 8JW, United Kingdom. peter.norman@nationwideisp.net
SOURCE: Expert Opinion on Therapeutic Patents, (2000) Vol. 10, No. 9, pp. 1415-1427.
Refs: 35
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 013 Dermatology and Venereology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Sep 2000
Last Updated on STN: 28 Sep 2000

AB The search for novel PDE4 inhibitors remains a highly active field for the pharmaceutical industry with 55 applications published in 1999. These efforts remain concentrated on the identification of compounds based upon catechol or phthalazine derivatives. Several applications suggest such compounds have utility for new indications such as leukaemia and pruritus. Clinical development of a number of compounds, led by cilomilast and roflumilast, is progressing steadily for indications that include COPD, asthma, psoriasis and dermatitis. This review highlights the novel structural classes of PDE4 inhibitors disclosed in the past year's patent applications and the clinical developments with PDE4 inhibitors.

L11 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:142112 BIOSIS
DOCUMENT NUMBER: PREV199900142112
TITLE: The in vivo activity of AWD 12-281, a potent PDE4 inhibitor for the treatment of allergic asthma.
AUTHOR(S): Marx, D.; Poppe, H.; Szelenyi, I.
CORPORATE SOURCE: Corporate Res. ASTA Med. AG, Arzneimittelwerk, Dresden, Germany
SOURCE: Journal of Allergy and Clinical Immunology, (Jan., 1999) Vol. 103, No. 1 PART 2, pp. S127. print.
Meeting Info.: 55th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. Orlando, Florida, USA. February 26-March 3, 1999. American Academy of Allergy, Asthma, and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 1999
Last Updated on STN: 31 Mar 1999

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=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      69.66      93.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -5.60      -5.60

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DICTIONARY FILE UPDATES:  18 JUN 2008  HIGHEST RN 1029146-45-9

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http://www.cas.org/support/stngen/stndoc/properties.html

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           186 AWD
        936573 12
          8636 281
L12          1 AWD 12-281
                 (AWD(W)12(W)281)

=> d L12 str cn rn

L12  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2008 ACS on STN
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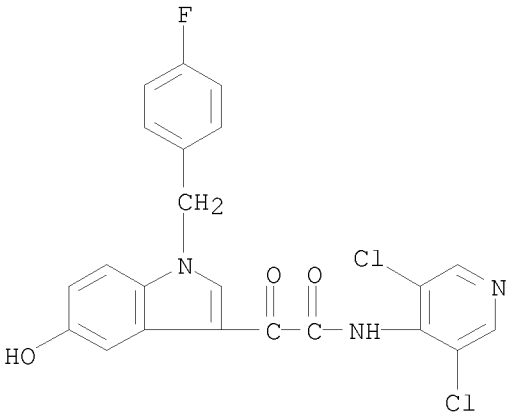

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (CA INDEX NAME)
OTHER NAMES:
CN AWD 12-281
CN GW 842470
RN 257892-33-4 REGISTRY

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	28.49	121.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-5.60

FILE 'CAPLUS' ENTERED AT 11:33:38 ON 19 JUN 2008
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FILE COVERS 1907 - 19 Jun 2008 VOL 148 ISS 25
FILE LAST UPDATED: 18 Jun 2008 (20080618/ED)

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http://www.cas.org/legal/infopolicy.html

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=> s 257892-33-4
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L14         59 L13


=> dup rem L14
PROCESSING COMPLETED FOR L14
L15          59 DUP REM L14 (0 DUPLICATES REMOVED)

=> s allergy or allergic or dermatitis
          51993 ALLERGY
           3810 ALLERGIES
          53031 ALLERGY
                (ALLERGY OR ALLERGIES)
          40035 ALLERGIC
             82 ALLERGICS
          40058 ALLERGIC
                (ALLERGIC OR ALLERGICS)
          20881 DERMATITIS
              9 DERMATITISES
          20883 DERMATITIS
                (DERMATITIS OR DERMATITISES)
L16       82108 ALLERGY OR ALLERGIC OR DERMATITIS

=> s L14 and L16
L17         19 L14 AND L16

=> s topical or skin
          50682 TOPICAL
             41 TOPICALS
          50701 TOPICAL
                (TOPICAL OR TOPICALS)
         281014 SKIN
          11007 SKINS
         287170 SKIN
                (SKIN OR SKINS)
L18      317846 TOPICAL OR SKIN

=> s L17 and L18
L19         15 L17 AND L18

=> d 1-15 L19 ibib abs

L19  ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2007:1242672  CAPLUS
DOCUMENT NUMBER:         147:491665
TITLE:                   dermatological and cosmetological compositions
                         containing MC1R agonists for modulating melanogenesis
INVENTOR(S):             Fisher, David E.; D'Orazio, John; Khaled, Mehdi
PATENT ASSIGNEE(S):      Dana-Farber Cancer Institute, Inc., USA
SOURCE:                  PCT Int. Appl., 123pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007123699	A1	20071101	WO 2007-US7935	20070329

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-787552P P 20060330
US 2006-841739P P 20060901

AB The present invention provides compns. comprising an MC1R agonist and methods using these compns. for inducing or inhibiting UV-independent pigmentation of human skin and/or for enhancing UV- dependent pigmentation of human skin.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:702698 CAPLUS
DOCUMENT NUMBER: 147:125811
TITLE: Combination comprising cyclooxygenase and lipooxygenase inhibitor for managing inflammation and associated disorders
INVENTOR(S): Jain, Rajesh; Jindal, Kour Chand
PATENT ASSIGNEE(S): Panacea Biotec Ltd., India
SOURCE: PCT Int. Appl., 37pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007072503	A2	20070628	WO 2006-IN496	20061218
WO 2007072503	A3	20071101		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: IN 2005-DE3431 A 20051221

AB This invention relates to pharmaceutical compns. comprising at least one analgesic and anti-inflammatory compound(s) that inhibits both

cyclooxygenase (COX) and lipooxygenase (LOX) as active agent in combination with at least one another active agent(s) optionally with other pharmaceutically, acceptable excipients is provided. Also described are process for preparation of such compns. and method of using such compns. for the management of inflammation and pain and/or other associated disorders. Thus, tablet was prepared containing licofelone 200 mg, nimesulide 100 mg, AvicelPH 101 50 mg, lactose monohydrate 35 mg, starch 1500 30 mg, sodium lauryl sulfate 20 mg, croscarmellose sodium 15 mg, silicone dioxide 5 mg, starch 20 mg, magnesium stearate 5 mg, talc 5 mg and purified water as needed.

L19 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:331227 CAPLUS
DOCUMENT NUMBER: 146:308239
TITLE: Highly selective phosphodiesterase 4 inhibitors for the treatment of allergic skin diseases and psoriasis
AUTHOR(S): Baeumer, Wolfgang; Hoppmann, Joachim; Rundfeldt, Chris; Kietzmann, Manfred
CORPORATE SOURCE: Department of Pharmacology, Toxicology, and Pharmacy, Foundation, University of Veterinary Medicine Hannover, Hannover, D-30559, Germany
SOURCE: Inflammation & Allergy: Drug Targets (2007), 6(1), 17-26
CODEN: IADTAQ; ISSN: 1871-5281
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The phosphodiesterase (PDE) 4 is the predominant cAMP degrading enzyme in a variety of inflammatory cells including eosinophils, neutrophils, macrophages, T cells and monocytes. In addition, this enzyme is expressed in non-immune cells such as keratinocytes and fibroblasts. Highly selective PDE4 inhibitors are currently under evaluation for the treatment of asthma and/or chronic obstructive pulmonary disease. Due to the broad anti-inflammatory/immunomodulatory action of PDE4 inhibitors, it has been proposed that PDE4 inhibitors might also be efficacious for skin disorders such as atopic dermatitis. Consequently, PDE4 inhibitors including cilomilast and AWD 12-281 have been tested in several models of allergic and irritant skin inflammation. These PDE4 inhibitors displayed strong anti-inflammatory action in models of allergic contact dermatitis in mice, in the arachidonic acid induced skin inflammation in mice and in ovalbumin sensitized guinea pigs. The determination of cytokines in skin homogenates revealed that both Th1 as well as Th2 cytokines are suppressed by PDE4 inhibitors, indicating an anti-inflammatory activity in both the Th2 dominated acute phase as well as the Th1 dominated chronic phase of atopic dermatitis. Due to the suppression of Th1 cytokines, activity can also be expected in psoriasis. Results of early clin. trials with both topically (cipamfylline, CP80,633) and systemically (CC-10004) active PDE4 inhibitors demonstrated efficacy in atopic dermatitis and in the case of CC-10004, also in psoriasis. AWD 12-281 (GW 842470) is currently under clin. evaluation for the topical treatment of atopic dermatitis. Results concerning clin. efficacy of this potent and selective PDE4 inhibitor are anxiously awaited.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1256669 CAPLUS
DOCUMENT NUMBER: 146:20293
TITLE: Novel medicament combinations for the treatment of

respiratory diseases
INVENTOR(S): Pieper, Michael P.; Schnapp, Andreas; Nickolaus, Peter
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 33pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060270667	A1	20061130	US 2006-420872	20060530
CA 2609429	A1	20061207	CA 2006-2609429	20060529
WO 2006128847	A2	20061207	WO 2006-EP62683	20060529
WO 2006128847	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1893203	A2	20080305	EP 2006-763340	20060529
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: EP 2005-104702 A 20050531
WO 2006-EP62683 W 20060529
OTHER SOURCE(S): MARPAT 146:20293
AB The present invention relates to new medicament combinations which contain in addition to one or more, preferably one, betamimetic, at least one anticholinergic and at least one PDE-IV inhibitor processes for preparing them and their use as pharmaceutical compns.

L19 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:365169 CAPLUS
DOCUMENT NUMBER: 144:419682
TITLE: Pharmaceutical compositions containing phosphodiesterase IV inhibitors and immunosuppressants
INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko; Ohshima, Etsuo
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041120	A1	20060420	WO 2005-JP18854	20051013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,				

SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2584261	A1	20060420	CA 2005-2584261	20051013
EP 1813284	A1	20070801	EP 2005-793647	20051013
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20080085858	A1	20080410	US 2007-576970	20070410
PRIORITY APPLN. INFO.:			JP 2004-299104 A	20041013
			JP 2005-113265 A	20050411
			WO 2005-JP18854 W	20051013

AB This invention relates to pharmaceutical compns. for the prevention and treatment of chronic skin diseases, comprising (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) an immunosuppressant, which are administered simultaneously or sep. with an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone (PDE-IV inhibitor) 20, tacrolimus (immunosuppressant) 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:364924 CAPLUS
DOCUMENT NUMBER: 144:398341
TITLE: Phosphodiesterase IV inhibitor and steroid combinations for the treatment of chronic skin disease
INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko; Ohshima, Etsuo
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041121	A1	20060420	WO 2005-JP18855	20051013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2584169	A1	20060420	CA 2005-2584169	20051013
EP 1810692	A1	20070725	EP 2005-793699	20051013
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
US 20070287689 A1 20071213 US 2007-576972 20070410
PRIORITY APPLN. INFO.: JP 2004-299103 A 20041013
JP 2005-113264 A 20050411
WO 2005-JP18855 W 20051013

AB It is intended to provide a remedy and/or a preventive for a chronic skin disease which comprises (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) a steroid drug, which are administered simultaneously or sep. at an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone 50, prednisolone 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:226501 CAPLUS
DOCUMENT NUMBER: 144:267237
TITLE: The phosphodiesterase 4 inhibitor AWD 12-281 is active in a new guinea-pig model of allergic skin inflammation predictive of human skin penetration and suppresses both Th1 and Th2 cytokines in mice
AUTHOR(S): Hoppmann, Joachim; Baeumer, Wolfgang; Galetzka, Christin; Hoefgen, Norbert; Kietzmann, Manfred; Rundfeldt, Chris
CORPORATE SOURCE: Department of Pharmacology, elbion AG, Radebeul, D-01445, Germany
SOURCE: Journal of Pharmacy and Pharmacology (2005), 57(12), 1609-1617
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The selective phosphodiesterase 4 (PDE4) inhibitor AWD 12-281 is structurally optimized for topical administration. It has potent effects in models of lung inflammation if administered as a dry powder inhalation. It has also demonstrated its anti-inflammatory property in a mouse model of cutaneous inflammation after topical administration. The aim of this study was to evaluate whether AWD 12-281 may be capable of penetrating human skin. Therefore a new guinea-pig model of allergic skin inflammation had to be developed. In ovalbumin-sensitized guinea-pigs, intracutaneous administration of ovalbumin results in a rapid development of allergic skin wheals. Topically administered AWD 12-281 was capable of reducing the development of wheals, indicating that this compound can penetrate the stratum corneum of guinea-pig skin as a predictor of human skin penetration. A secondary aim was the evaluation of a T cell subtype preference of AWD 12-281 since PDE4 inhibitors are said to preferentially inhibit Th2-type cytokines. Therefore, the effects of AWD 12-281 on a broad spectrum of Th1- and Th2-type cytokines were studied in tissue homogenates after allergen challenge in sensitized mice and in supernatants of anti CD3/anti-CD28-stimulated peripheral blood mononuclear cells (PBMCs). In both models, AWD 12-281 suppressed both T cell subtype cytokines indicating a broad spectrum activity of AWD 12-281. A further issue was to determine the duration of action and the concentration-response relation of the topical activity of AWD 12-281 using a model of acute local inflammation - the arachidonic-acid-induced mouse ear edema. The compound

exhibited a dose-dependent effect with a minimally effective concentration of 0.3%; after repeated administration the minimally effective concentration was 0.03%. A single administration of a 3% solution resulted in significant suppression of inflammation even 48 h after treatment. In conclusion, our results indicate that AWD 12-281 is a very promising drug candidate not only for the treatment of lung inflammation using inhalative administration but also for the treatment of atopic dermatitis.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:149262 CAPLUS
DOCUMENT NUMBER: 144:239931
TITLE: Pharmaceutical compositions for the treatment of respiratory and gastrointestinal disorders
INVENTOR(S): Jung, Birgit; Himmelsbach, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co. KG
SOURCE: PCT Int. Appl., 321 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015775	A2	20060216	WO 2005-EP8385	20050803
WO 2006015775	A3	20070518		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20060035893	A1	20060216	US 2005-189643	20050726
CA 2575541	A1	20060216	CA 2005-2575541	20050803
EP 1784224	A2	20070516	EP 2005-773706	20050803
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008509177	T	20080327	JP 2007-525227	20050803

PRIORITY APPLN. INFO.: EP 2004-18808 A 20040807
WO 2005-EP8385 W 20050803

OTHER SOURCE(S): MARPAT 144:239931

AB The present invention relates to novel pharmaceutical compns. comprising at least 1 EGFR kinase inhibitor and at least one addnl. active compound selected from β-2 mimetics, steroids, PDE-IV inhibitors, p38 MAP kinase inhibitors, NK1 antagonists and endothelin-antagonists, processes for preparing the compns. and the use thereof as drugs in the treatment of respiratory or gastrointestinal complaints, as well as inflammatory diseases of the joints, the skin or the eyes. Thus, an inhalable powder contained an EGFR kinase inhibitor 150, formoterol fumarate dihydrate 50, and lactose 12,300 mg/capsule.

L19 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

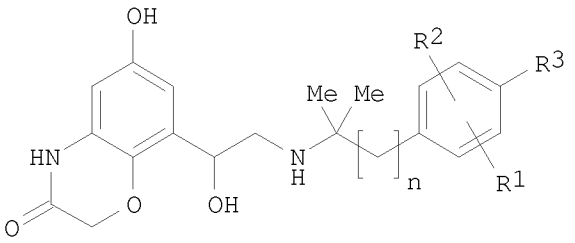
ACCESSION NUMBER: 2005:1155523 CAPLUS
DOCUMENT NUMBER: 143:416252
TITLE: Novel medicament combinations for the treatment of respiratory diseases
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050239778	A1	20051027	US 2005-109094	20050419
DE 102004019540	A1	20051110	DE 2004-102004019540	20040422
DE 102004052987	A1	20060504	DE 2004-102004052987	20041103
AU 2005235419	A1	20051103	AU 2005-235419	20050418
CA 2559699	A1	20051103	CA 2005-2559699	20050418
WO 2005102349	A1	20051103	WO 2005-EP4073	20050418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1781298	A1	20070509	EP 2005-739576	20050418
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101035540	A	20070912	CN 2005-80012621	20050418
BR 2005010080	A	20071016	BR 2005-10080	20050418
JP 2007533683	T	20071122	JP 2007-508805	20050418
MX 2006PA11721	A	20061211	MX 2006-PA11721	20061010
NO 2006005060	A	20061121	NO 2006-5060	20061102
KR 2007015592	A	20070205	KR 2006-724528	20061122

PRIORITY APPLN. INFO.:

DE 2004-102004019540A		20040422
US 2004-578542P	P	20040610
DE 2004-102004052987A		20041103
EP 2005-2496	A	20050207
WO 2005-EP4073	W	20050418

OTHER SOURCE(S): MARPAT 143:416252
GI



I

AB The present invention relates to a pharmaceutical composition comprising one or

more compds. of formula I wherein n denotes 1 or 2; R1 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R2 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R3 denotes C1-C4-alkyl, OH, halogen, -O-C1-C4-alkyl, -O-C1-C4-alkylene-COOH, -O-C1-C4-alkylene-CO-O-C1-C4-alkyl, and at least one other active substance for the treatment of respiratory diseases. The second active substance can by an anticholinergic, a phosphodiesterase IV inhibitor, a steroid, a LTD4 antagonist or an EGFR inhibitor.

L19 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:203704 CAPLUS
DOCUMENT NUMBER: 140:229455
TITLE: Combination of glucocorticoids and PDE-4-inhibitors for treating respiratory diseases, allergic diseases, asthma and COPD
INVENTOR(S): Locher, Mathias; Hermann, Robert
PATENT ASSIGNEE(S): Viatris G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019984	A1	20040311	WO 2003-EP8607	20030804
W: AU, BR, CA, CN, CO, CZ, GE, HR, ID, IL, IN, JP, KR, LT, LV, MD, MK, MX, NO, NZ, PL, SG, UA, US, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2492645	A1	20040311	CA 2003-2492645	20030804
AU 2003255365	A1	20040319	AU 2003-255365	20030804
EP 1526870	A1	20050504	EP 2003-790851	20030804
EP 1526870	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK				
CN 1674939	A	20050928	CN 2003-819057	20030804
JP 2005539042	T	20051222	JP 2004-531853	20030804
AT 361076	T	20070515	AT 2003-790851	20030804
ES 2285238	T3	20071116	ES 2003-790851	20030804
MX 2005PA01573	A	20050425	MX 2005-PA1573	20050209
US 20050288265	A1	20051229	US 2005-523802	20050209
IN 2005KN00155	A	20060421	IN 2005-KN155	20050209
NO 2005001212	A	20050308	NO 2005-1212	20050308
HR 2005000224	B1	20071231	HR 2005-224	20050308
HK 1078463	A1	20071026	HK 2005-110373	20051118

PRIORITY APPLN. INFO.:		DE 2002-10236688 A	20020809
		WO 2003-EP8607 W	20030804

AB The invention relates to a novel combination of a glucocorticoid, especially loteprednol, and at least one phosphodiesterase-4 inhibitor (PDE-4-inhibitor), especially hydroxyindole-derivative N-(3,5-dichloropyridine-4-yl)-2-[1-(4-fluorbenzyl)-5-hydroxyindole-3-yl]-2-oxoacetamide, for a simultaneous, sequential or sep. administration in the treatment of respiratory diseases, allergic diseases, asthma and chronic obstructive pulmonary diseases (COPD). Formulation of glucocorticoids and PDE-4-inhibitors can be prepared sep. and applied at the same time or at different times during the day; also combinations can be formulated.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:130977 CAPLUS
DOCUMENT NUMBER: 140:281023
TITLE: Anti-inflammatory potential of the selective phosphodiesterase 4 inhibitor N-(3,5-dichloro-pyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxy-indole-3-yl]-glyoxylic acid amide (AWD 12-281), in human cell preparations
AUTHOR(S): Draheim, Regina; Egerland, Ute; Rundfeldt, Chris
CORPORATE SOURCE: Departments of Pharmacology and Molecular Biology, Elbion AG, Radebeul, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 308(2), 555-563
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AWD 12-281 is a potent (IC50 = 9.7 nM) and highly selective inhibitor of the phosphodiesterase 4 (PDE4) isoenzyme with low affinity to the high-affinity rolipram-binding site. The compound was optimized for topical treatment of asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis. The aim of the present study was to assess the effect of AWD 12-281 in human inflammatory cells. Peripheral blood mononuclear cells (PBMCs), diluted whole blood, and human nasal polyp cells derived from surgically resected nasal polyps from patients with polyposis comprise sources of target tissue cells that can be used to predict anti-inflammatory effects in patients. AWD 12-281 was capable of suppressing the production of cytokines in stimulated PBMCs: interleukin-2 (IL-2, phytohemagglutinin stimulation), IL-5 (Con A stimulation), IL-5 and IL-4 (anti-CD3/anti-CD28 co-stimulation), and lipopolysaccharide-stimulated release of tumor necrosis factor α (TNFα). The corresponding values for half-maximum inhibition, EC50, for AWD 12-281 were within a narrow range (46-121 nM). Comparing the effect of AWD 12-281 with roflumilast, cilomilast (SB 207499), rolipram (RPR-73401), and 1-(3-nitrophenyl)-3-(4-pyridylmethyl)pyrido[2,3-d]pyrimidin-2,4(1H,3H)-dione (RS-25344-000), it could be shown that the PDE4 inhibitory activity was closely correlated with inhibitory potential as measured by the above-described assays. AWD 12-281 was also shown to suppress TNFα release in dispersed nasal polyps (EC50 = 111 nM) and in diluted whole blood (EC50 = 934 nM). The reduced activity in human blood may be related to high plasma protein binding. Currently, phase II clin. studies are under way to evaluate the therapeutic potential of AWD 12-281 in asthma, COPD, and allergic rhinitis.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:60309 CAPLUS
DOCUMENT NUMBER: 140:105273
TITLE: Topical treatment of skin diseases
INVENTOR(S): Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann, Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen, Norbert
PATENT ASSIGNEE(S): Elbion AG, Germany
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004006920	A1	20040122	WO 2003-EP7514		20030710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 20040038958	A1	20040226	US 2003-611649		20030701
CA 2492093	A1	20040122	CA 2003-2492093		20030710
AU 2003254332	A1	20040202	AU 2003-254332		20030710
BR 2003012696	A	20050426	BR 2003-12696		20030710
EP 1531818	A1	20050525	EP 2003-763810		20030710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1681500	A	20051012	CN 2003-821520		20030710
JP 2005537262	T	20051208	JP 2004-520586		20030710
NZ 537482	A	20060929	NZ 2003-537482		20030710
ZA 2005000108	A	20050223	ZA 2005-108		20050106
MX 2005PA00486	A	20050722	MX 2005-PA486		20050111
NO 2005000718	A	20050401	NO 2005-718		20050210
PRIORITY APPLN. INFO.:			US 2002-395221P	P	20020711
			WO 2003-EP7514	W	20030710

OTHER SOURCE(S): MARPAT 140:105273

AB The present invention relates to a method for the treatment of an inflammatory and/or allergic skin disease comprising topically administering a substituted hydroxy indole which is a phosphodiesterase 4 inhibitor. Examples are provided of the topical effectiveness of AWD 12-281 and cilomilast in dermal immunol. inflammation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:695438 CAPLUS

DOCUMENT NUMBER: 140:87294

TITLE: AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in the prevention and treatment of inflammatory reactions in a model of allergic dermatitis

AUTHOR(S): Baeumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Rundfeldt, Chris; Kietzmann, Manfred

CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, School of Veterinary Medicine, Hannover, D-30559, Germany

SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(8), 1107-1114
CODEN: JPPMAB; ISSN: 0022-3573

PUBLISHER: Pharmaceutical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a phosphodiesterase 4 inhibitor, which is optimized for topical administration, was tested in a model of allergic dermatitis in mice. To obtain an

allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by topical administration of TDI onto the mice ears. AWD 12-281 was tested for its anti-inflammatory potential by oral, i.p. and topical administration. The phosphodiesterase 4 inhibitor, cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate, were used as reference compds. Given orally and i.p. 2 h before as well as 5 and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4, interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be potent in the prevention and treatment of allergic/inflammatory skin diseases.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:495906 CAPLUS

DOCUMENT NUMBER: 138:117605

TITLE: Effects of the phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on the inflammatory reaction in a model of allergic dermatitis

AUTHOR(S): Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Ehinger, Britt; Kietzmann, Manfred

CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany

SOURCE: European Journal of Pharmacology (2002), 446(1-3), 195-200
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by topical administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups of mice were treated topically (ear skin) with SB 207499 or AWD 12-281. There was a significant ear swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB 207499 and AWD 12-281 inhibited this swelling significantly 8, 16, 24 and 48 h after the challenge. For biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited significantly the secretion of interleukin 1β induced by toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-281 and SB 204799.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:420229 CAPLUS
DOCUMENT NUMBER: 138:18980
TITLE: AWD 12-281
AUTHOR(S): Kuss, H.; Hofgen, N.; Egerland, U.; Heer, S.; Marx, D.; Szelenyi, I.; Schupke, H.; Gasparic, A.; Olbrich, M.; Hempel, R.; Hartenhauer, H.; Krone, D.; Berthold, K.; Kronbach, T.; Rundfeldt, C.
CORPORATE SOURCE: Arzneimittelwerk Dresden GmbH, Radebeul, D-01445, Germany
SOURCE: Drugs of the Future (2002), 27(2), 111-116
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Airway diseases such as bronchial asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases whose prevalence is increasing. Current research concerned with developing effective treatments for these conditions have focused on the search for alternatives to the standard corticosteroid antiinflammatory therapy. Selective phosphodiesterase 4 (PDE4) inhibitors have received a considerable amount of attention due to their ability to suppress the functions of several cell types involved in allergic and inflammatory disorders. The selective PDE4 inhibitor AWD 12-281 is the result of a pharmacophore-based synthesis program wherein the optimization process was supported by ligand-based drug design methods. AWD 12-281 was selected for further development for its high affinity and selectivity for the human PDE4 isoenzyme and due to its potent activity and excellent tolerability in models of allergic rhinitis, asthma and COPD, especially after topical treatment.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST	62.13	184.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.00	-17.60

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